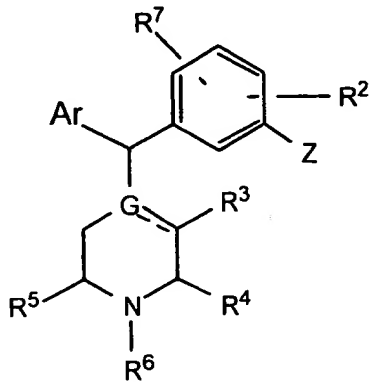
ABSTRACT OF THE DISCLOSURE

A method of reducing, treating or preventing drug-mediated respiratory depression, muscle rigidity, or nausea/vomiting in an animal, incident to the administration to said animal of a mixed delta/mu opioid agonist or a respiratory depression-mediating drug, comprising administering to the animal receiving said drug an effective amount of a delta receptor agonist compound. The delta agonist compound may comprise a compound of the formula:



(I)

wherein:

Ar is a 5- or 6-member carbocyclic or heterocyclic aromatic ring with atoms selected from the group consisting of carbon, nitrogen, oxygen and sulfur, and having on a first carbon atom thereof a substituent Y and on a second ring carbon thereof a substituent R^1,

Y is selected from the group consisting of:

hydrogen;

halogen;

C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl;

C_1-C_6 haloalkyl;

C_1-C_6 alkoxy;

C_3-C_6 cycloalkoxy;

sulfides of the formula SR^8 where R^8 is C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, arylalkyl having a C_5-C_{10} aryl moiety and an C_1-C_6 alkyl moiety, or C_5-C_{10} aryl;

sulfoxides of the formula SOR^8 where R^8 is the same as above;

sulfones of the formula SO_2R^8 where R^8 is the same as above;

nitrile;

C_1-C_6 acyl;

alkoxycarbonylamino (carbamoyl) of the formula $NHCO_2R^8$ where R^8 is the same as above;

carboxylic acid, or an ester, amide, or salt thereof;

aminomethyl of the formula $CH_2NR^9R^{10}$ where R^9 and R^{10} may be the same or different, and may be hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_2-C_6 hydroxyalkyl, C_2-C_6 methoxyalkyl, C_3-C_6 cycloalkyl, or C_5-C_{10} aryl, or R^9 and R^{10} together may form a ring of 5 or 6 atoms, the ring atoms selected from the group consisting of N and C;

carboxamides of the formula $CONR^9R^{10}$ where R^9 and R^{10} are the same as above, or C_2-C_{30} peptide conjugates thereof; and

sulfonamides of the formula $SO_2NR^9R^{10}$ where R^9 and R^{10} are the same as above;

Z is selected from the group consisting of:

hydroxyl, and esters thereof;

hydroxymethyl, and esters thereof; and

amino, and carboxamides and sulfonamides thereof;

G is carbon or nitrogen;

R^1 is hydrogen, halogen, or C_1-C_4 alkyl, C_2-C_4 alkenyl, C_1-C_4 alkynyl;

R^2 is hydrogen, halogen, or C_1-C_4 alkyl, C_2-C_4 alkenyl, C_1-C_4 alkynyl;

R^3, R^4 and R^5 may be the same or different, and are independently selected from hydrogen and methyl, and wherein at least one of R^3, R^4 or R^5 is not hydrogen, subject to the proviso that the total number of methyl groups does not exceed two, or any two of R^3, R^4 and R^5 together may form a bridge of 1 to 3 carbon atoms;

R^6 is selected from the group consisting of:

hydrogen;

C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl;

C_3-C_6 cycloalkyl;

arylalkyl having C_5-C_{10} aryl and C_1-C_6 alkyl moieties;

alkoxyalkyl having C_1-C_4 alkoxy and C_1-C_4 alkyl moieties;

C_2-C_4 cyanoalkyl;

C_2-C_4 hydroxyalkyl;

aminocarbonylalkyl having a C_1-C_4 alkyl moiety; and

$R^{12}COR^{13}$, where R^{12} is C_1-C_4 alkylene, and R^{13} is C_1-C_4 alkyl or C_1-C_4 alkoxy; and

R^7 is hydrogen or fluorine,

or a pharmaceutically acceptable ester or salt thereof.